

P26669.A03

Application No. 10/524,420

IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Reiko KAWAMURA

Group Art Unit : Not Yet Assigned

Appl. No. : 10/524,420

(U.S. National Stage of PCT/JP03/10440)

Examiner : Not Yet Assigned

I.A. Filed : August 19, 2003

Conf. No.: 6272

For : SOFT CAPSULE PREPARATION

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
U.S. Patent and Trademark Office  
Customer Service Window, Mail Stop AMENDMENT  
Randolph Building  
401 Dulany Street  
Alexandria, VA 22314

Sir :

In accordance with the duty of disclosure under 37 C.F.R. §§1.56 and 1.97-1.98, and supplemental to the Information Disclosure Statement filed August 2, 2005, Applicant hereby brings the following information to the attention of the Examiner:

- (1) U.S. Patent No. 6,369,251 B2;
- (2) U.S. Patent No. 6,984,742 B2;
- (3) US 2005/0250671 A1, which is a national stage of PCT/JP01/03442 and published as WO 01/80854 A1;
- (4) US 2006/0063838;
- (5) US 2006/0094784 A1, and is a National Stage of PCT/JP03/06116 and published as WO 03/097034 A1;

- (6) Nariaki NAKAMURA et al., "Apoptosis in Human Hepatoma Cell Line Induced by 4,5-Didehydrogeranylgeranoic Acid (Acyclic Retinoid) Via Down-Regulation of Transforming Growth Factor- $\alpha$ ," Biochemical and Biophysical Research Communications, Vol. 219, No. 1, pp. 100-104 (1996);
- (7) JP 63-32058 B2 (EISAI CO., LTD), accompanied by an English language abstract (provided by Patent Abstracts of Japan) of the corresponding published application JP 56-140949, published 4 November 1981 and family members U.S. Patent Nos. 4,346,109, 4,917,829, and 4,988,732;
- (8) M. OKUNO et al., "Retinoids Exacerbate Rat Liver Fibrosis by Inducing the Activation of latent TGF- $\beta$  in Liver Stellate Cells," Hepatology (Philadelphia), Vol. 26, No. 4, pp. 913-921 (1997);
- (9) DI BISCEGLIE A.M. et al., "Hepatocellular Carcinoma," Hepatology, Vol. 28, No. 4, pp. 1161-1165 (1998);
- (10) ISHIWARI, K., "The Effects of a Synthetic Retinoid on Phenotypic Expression of Cultured Mesangial Cells," Kyoto-furitsu Ika Daigaku Zasshi, Vol. 106, No. 3, pp. 273-283 (1997).
- (11) U.S. Patent No. 4,757,140;
- (12) U.S. Patent No. 4,841,038;
- (13) U.S. Patent No. 4,888,439;
- (14) U.S. Patent No. 5,852,057;
- (15) EP 0 054 732 A1, and family member U.S. Patent No. 4,655,973;

- (16) EP 0 194 693 A1, and family members U.S. Patent Nos. 4,788,330, and 4,883,916;
- (17) GB 781,809;
- (18) JP 63-34855 B2 (EISAI CO., LTD), accompanied by an English language abstract (provided by Patent Abstracts of Japan) of the corresponding published application, JP 57-106638, published 2 July 1982 and family member U.S. Patent No. 4,655,973;
- (19) JP 2000-122974;
- (20) WO 94/22818;
- (21) P. ELLINGHAUS et al., "Phytanic Acid Activates the Peroxisome Proliferator-Activated Receptor  $\alpha$  (PPAR $\alpha$ ) in Sterol Carrier Protein 2- /Sterol Carrier Protein x-deficient Mice," J. Biol. Chem., Vol. 274, No. 5, pp. 2766-2772 (January 29, 1999);
- (22) S.A. KLIEWER et al., "Fatty acids and eicosanoids regulate gene expression through direct interactions with peroxisome proliferators-activated receptors  $\alpha$  and  $\gamma$ ," Proc. Natl. Acad. Sci. U.S.A., Vol. 94, No. 9, pp. 4318-4323 (April 1997);
- (23) M. GÖTTLICHER et al., "Structural and Metabolic Requirements for Activators of the Peroxisome Proliferator-Activated Receptor," Biochem. Pharmacol., Vol 46, No. 12, pp. 2177-2184 (1993);
- (24) I. ISSEMAN et al., "The peroxisome proliferators-activated receptor:retinoid X receptor heterodimer is activated by fatty acids

- and fibrate hypolipidaemic drugs," J. Mol. Endocrinol., Vol. 11, No. 1, pp. 37-47 (1993);
- (25) G.M. REAVEN, "Role of Insulin Resistance in Human Disease," Diabetes, Vol. 37, pp. 1595-1607 (1988);
- (26) I. ISSEMAN et al., "Activation of a member of the steroid hormone receptor superfamily by peroxisome proliferators," Nature, Vol. 347, pp. 645-650 (1990);
- (27) J.M. LEHMANN et al., "An Antidiabetic Thiozolidinedione Is a High Affinity Ligand for Peroxisome Proliferator-activated Receptor  $\gamma$  (PPAR $\gamma$ )," J. Biol. Chem. Vol. 270, No. 22, pp. 12953-12956 (1995);
- (28) A.R. SALTIEL et al., "Thiozolidinediones in the Treatment of Insulin Resistance and Type II Diabetes," Diabetes, Vol. 45, pp. 1661-1669 (1996);
- (29) Rinshu IYAKU, "Liver Dysfunction Associated with Troglitazone (Noscal®)," Vol. 14, pp. 461-466 (1998);
- (30) Remington: The Science and Practice of Pharmacy, Mack Publishing Co., Nineteenth Edition, Vol. 1, Chapter 48, "The Introduction of New Drugs", pages 795-808 (1995);
- (31) K. TAGO et al., "A Practical Total Synthesis of Plaunotol via Highly Z-selective Wittig Olefination of  $\alpha$ -acetal ketones," J. Chem. Soc. Perkin Trans. 1, pp. 2073-2078 (2000);

- (32) W.C. STILL et al., "Direct Synthesis of Z-Unsaturated Esters. A Useful Modification of the Horner-Emmons Olefination," *Tetrahedron Letters*, Vol. 24, No. 41, pp. 4405-4408 (1983);
- (33) T. KAJIWARA et al., "Stereoselective Synthesis of Ectocarpene and Its Antipode via Microbiological Asymmetric Hydrolysis," *Agric. Biol. Chem.*, Vol. 45, pp. 1461-1466 (1981);
- (34) *Chinese Journal of Applied Chemistry*, Vol. 5, 1988, pp. 70-71;
- (35) R. BODEN, "A Mild Method for Preparing trans-Alkenes; Crown Ether Catalysis of the Wittig Reaction," *Synthesis*, p. 784 (1975);
- (36) G. BELLUCCI et al., "Crown Ether Catalyzed Stereospecific Synthesis of Z- and E-Stilbenes by Wittig Reaction in a Solid-Liquid Two-Phases System," *Tetrahedron Letters*, Vol. 37, No. 24, pp. 4225-4228 (1996);
- (37) M. MIKOLAJCZYK et al., "Synthesis of  $\alpha,\beta$ -Unsaturated Sulphides, Sulphoxides, and Sulphones by the Horner-Wittig Reaction in Two-Phase System Catalysed by Quaternary Ammonium Salts and Crown Ethers," *Synthesis*, pp. 278-280 (1975);
- (38) *Izv. Akad. Nauk SSSR, Khim.*, 1990, pp. 2544-2550;
- (39) *Izv. Akad. Nauk SSSR, Khim.*, 1988, pp. 2382-2385;
- (40) *Izv. Akad. Nauk SSSR, Khim.*, 1988, pp. 2377-2382;
- (41) R.N. GEDYE et al., "The Stereochemistry of the Wittig Reactions of Allylic Phosphoranes and Phosponate Esters with Aldehydes," *Can. J. Chem.*, Vol. 55, pp. 1218-1228 (1977); and

(42) K. ASHIZAWA et al., "The Crystal Structure of 3,7,11,15-Tetramethyl-2,4,6,10,14- All Trans-Hexadecapentaenoic Acid (E-5166)," Chem. Pharm. Bull., Vol. 33, No. 7, pp. 3062-3064 (1985).

In accordance with 37 C.F.R 1.98, copies of the U.S. patents and U.S. published patent applications are not enclosed herewith. However, if any copies are needed, the Examiner is respectfully requested to contact the undersigned.

Copies of the above-noted documents, except for U.S. Patents and U.S. Patent Publications, are enclosed together with a duly completed Form PTO-1449. The Examiner is accordingly requested to consider each of these documents, and to make them of record in this application by initialing in the appropriate spaces on the Form PTO-1449. Applicant respectfully requests that the Examiner include a copy of the initialed Form PTO-1449 with the next communication from the U.S. Patent and Trademark Office.

Applicants note that while this Information Disclosure Statement is being filed more than three months from the filing date, Applicants have not received an action on the merits from the U.S. Patent and Trademark Office. Accordingly, consideration of the enclosed document is required under 37 C.F.R. 1.97(b)(3).

However, if an action on the merits has been mailed prior to the filing date of this Information Disclosure Statement, Applicants hereby authorize the charging of any required fees necessary for consideration of the documents cited herein to Deposit Account No. 19-0089.

Should there be any questions, the Examiner is invited to contact the undersigned at the below listed telephone number.

Respectfully Submitted,  
Reiko KAWAMURA

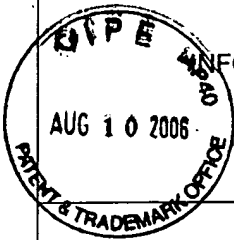


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FORM PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
P26669Application No.  
10/524,420INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT

(Use several sheets if necessary)

Applicant  
Reiko KAWAMURAFiling Date  
August 19, 2003Group  
Unknown

## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|-----------------|------|------|-------|----------|-------------------------------|
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| DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION<br>YES NO |
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| 1  | Nariaki NAKAMURA et al., "Apoptosis in Human Hepatoma Cell Line Induced by 4,5-Didehydrogeranylgeranoic Acid (Acyclic Retinoid) Via Down-Regulation of Transforming Growth Factor- $\alpha$ ," Biochemical and Biophysical Research Communications, Vol. 219, No. 1, pp. 100-104 (1996). |
| 2  | M. OKUNO et al., "Retinoids Exacerbate Rat Liver Fibrosis by Inducing the Activation of latent TGF- $\beta$ in Liver Stellate Cells," Hepatology (Philadelphia), Vol. 26, No. 4, pp. 913-921 (1997).   |
| 3  | DI BISCEGLIE A.M. et al., "Hepatocellular Carcinoma," Hepatology, Vol. 28, No. 4, pp. 1161-1165 (1998).  |
| 4  | ISHIWARI, K., "The Effects of a Synthetic Retinoid on Phenotypic Expression of Cultured Mesangial Cells," Kyoto-furitsu Ika Daigaku Zasshi, Vol. 106, No. 3, pp. 273-283 (1997).   |
| 5  | P. ELLINGHAUS et al., "Phytanic Acid Activates the Peroxisome Proliferator-Activated Receptor $\alpha$ (PPAR $\alpha$ ) in Sterol Carrier Protein 2-/Sterol Carrier Protein x-deficient Mice," J. Biol. Chem., Vol. 274, No. 5, pp. 2766-2772 (January 29, 1999).                        |
| 6  | S.A. KLIEWER et al., "Fatty acids and eicosanoids regulate gene expression through direct interactions with peroxisome proliferators-activated receptors $\alpha$ and $\gamma$ ," Proc. Natl. Acad. Sci. U.S.A., Vol. 94, No. 9, pp. 4318-4323 (April 1997).                             |
| 7  | M. GÖTTLICHER et al., "Structural and Metabolic Requirements for Activators of the Peroxisome Proliferator-Activated Receptor," Biochem. Pharmacol., Vol. 46, No. 12, pp. 2177-2184 (1993).  |
| 8  | I. ISSEMANN et al., "The peroxisome proliferators-activated receptor:retinoid X receptor heterodimer is activated by fatty acids and fibrates hypolipidaemic drugs," J. Mol. Endocrinol., Vol. 11, No. 1, pp. 37-47 (1993).  |
| 9  | G.M. REAVEN, "Role of Insulin Resistance in Human Disease," Diabetes, Vol. 37, pp. 1595-1607 (1988).   |
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| 12 | A.R. SALTIEL et al., "Thiozolidinediones in the Treatment of Insulin Resistance and Type II Diabetes," Diabetes, Vol. 45, pp. 1661-1669 (1996).  |
| 13 | Rinshu IYAKU, "Liver Dysfunction Associated with Troglitazone (Noscalt®)," Vol. 14, pp. 461-466 (1998);  |
| 14 | Remington: The Science and Practice of Pharmacy, Mack Publishing Co., Nineteenth Edition, Vol. 1, Chapter 48, "The Introduction of New Drugs", pages 795-808 (1995).   |

EXAMINER

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|---|--------------------------------|-------------------------------|
| FORM PTO-1449<br><br>U.S. Department of Commerce<br>Patent and Trademark Office<br><br><b>INFORMATION DISCLOSURE STATEMENT<br/>         BY APPLICANT</b><br>(Use several sheets if necessary) | Atty. Docket No.<br>P26669     | Application No.<br>10/524,420 |
|   | Applicant<br>Reiko KAWAMURA    |                               |
|   | Filing Date<br>August 19, 2003 | Group<br>Unknown              |

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## FOREIGN PATENT DOCUMENTS

| DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION<br>YES NO |
|-----------------|------|---------|-------|----------|-----------------------|
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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

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| 16 | W.C. STILL et al., "Direct Synthesis of Z-Unsaturated Esters. A Useful Modification of the Horner-Emmons Olefination," Tetrahedron Letters, Vol. 24, No. 41, pp. 4405-4408 (1983).  |
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| 22 | M. MIKOLAJCZYK et al., "Synthesis of $\alpha,\beta$ -Unsaturated Sulphides, Sulphoxides, and Sulphones by the Horner-Wittig Reaction in Two-Phase System Catalysed by Quaternary Ammonium Salts and Crown Ethers," Synthesis, pp. 278-280 (1975). |
| 23 | Izv. Akad. Nauk SSSR, Khim., 1990, pp. 2544-2550.   |
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| 27 | K. ASHIZAWA et al., "The Crystal Structure of 3,7,11,15-Tetramethyl-2,4,6,10,14- All Trans-Hexadecapentaenoic Acid (E-5166)," Chem. Pharm. Bull., Vol. 33, No. 7, pp. 3062-3064 (1985).   |
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| FORM PTO-1449   | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.<br>P26669     | Application No.<br>10/524,420 |
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|                     |      | 4 7 5 7 1 4 0   | 07/1288  | DELUCA et al.   |       |          |                               |
|                     |      | 4 3 4 6 1 0 9   | 08/24/82 | YAMATSU et al.  |       |          |                               |
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|                     |      | 4 8 4 1 0 3 8   | 06/20/89 | DELUCA et al.   |       |          |                               |
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|  |      | DOCUMENT NUMBER | DATE     | COUNTRY        | CLASS | SUBCLASS | TRANSLATION<br>YES NO |
|--|------|-----------------|----------|----------------|-------|----------|-----------------------|
|  | 01   | / 8 0 8 5 4     | 11/01/01 | W.I.P.O        |       |          |                       |
|  | 56   | - 1 4 0 9 4 9   | 11/04/81 | JAPAN          |       |          |                       |
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|  | 22 | English language Abstract of JP 56-140949. |
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|  |    |  |

**EXAMINER****DATE CONSIDERED**

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.